

Acute relative lymphopenia is associated with poor survival in glioblastoma patients following postoperative chemo-radiotherapy

Roberto Mapelli¹, Chiara Julita¹, Sofia Paola Bianchi¹, Nicolò Gallina¹, Raffaella Lucchini¹, Martina Midulla¹, Flavia Puci¹, Jessica Saddi ¹, Sara Trivellato², Denis Panizza², Elena De Ponti², Stefano Arcangeli (ORCID id: <https://orcid.org/0000-0003-3880-8876>)¹

¹ Department of Radiation Oncology, University of Milan Bicocca and San Gerardo Hospital – Monza (Italy)

² Department of Medical Physics, San Gerardo Hospital – Monza (Italy)

Strahlentherapie und Onkologie

Corresponding author: Roberto Mapelli (ORCID id: <https://orcid.org/0000-0003-1530-3138>; e-mail address: r.mapelli.95@gmail.com; r.mapelli4@campus.unimib.it)

Features	AAL	Non-AAL	p-value
Number of patients	31	26	
Clinical characteristics			
Sex male (%)	15 (48.4%)	16 (61.5%)	0.234 ^c
Age ^a	62 (54.0 – 68.0)	59 (51.0– 69.3)	0.395 ^d
Macroscopic radical surgery (%)	8 (25.8%)	8 (30.8%)	0.615 ^c
Time b/w surgery and RT ≥ 6 weeks (%)	26 (83.9%)	23 (88.5%)	0.458 ^c
Steroid dose 1-month FUP ≥ 4 mg/die (%)	12 (38.7%)	17 (65.4%)	*0.040 ^c
CT pre-RT (%)	18 (58.1%)	16 (61.5%)	0.503 ^c
CT/RT concomitant (%)	31 (100%)	26 (100%)	NA
Concomitant CT interrupted	5 (16.1%)	1 (3.8%)	0.142 ^c
Pathological characteristics			
MGMT: hypermethylated (%)	13 (52.0%)	9 (52.9%)	0.601 ^c
MGMT: non-hypermethylated (%)	12 (48.0%)	8 (47.1%)	
Dosimetric characteristics			
VMAT (%)	3 (9.7%)	2 (7.7%)	0.585 ^c
GTV ^b	62.9 cm ³ (39.7-83.0)	74.2 cm ³ (41.4-101.2)	0.202 ^d
CTV ^b	124.1 cm ³ (98.4-157.5)	154.1 cm ³ (123.2-190.6)	*0.034 ^d
PTV ^b	209.3 cm ³ (172.9-248.8)	241.3 cm ³ (197.5-294.5)	*0.038 ^d
PTV			
Dmean ^b	60.3 Gy (60.1-60.6)	60.5 Gy (60.1-60.8)	0.223 ^d
D98% ^b	57.4 Gy (56.5-58.1)	57.5 Gy (55.3-57.9)	0.553 ^d
D95% ^b	58.3 Gy (57.7-58.8)	58.1 Gy (57.1-58.6)	0.414 ^d
OARs			
D50% brainstem ^b	25.3 Gy (13.2-27.5)	14.2 Gy (4.3-28.7)	0.298 ^d
V50 brainstem ^b	8.9% (1.6-15.9)	7.6% (0.4-14.9)	0.803 ^d
D2% brainstem ^b	57.2 Gy (45.8-58.8)	56.3 Gy (40.0-58.1)	0.476 ^d
D2% chiasm ^b	35.5 Gy (18.0-55.1)	26.3 Gy (7.4-54.9)	0.415 ^d
Brain			
V50 ^b	21.6% (16.9-25.4)	25.5% (20.1-32.9)	*0.025 ^d
Dmean ^b	25.2 Gy (20.6-27.3)	26.6 Gy (21.2-31.1)	0.173 ^d
D98% ^b	1.1 Gy (0.7-1.4)	1.3 Gy (0.8-1.7)	0.286 ^d
D2% ^b	61.7 Gy (61.2-61.9)	62.0 Gy (61.6-62.5)	*0.021 ^d
Hypothalamus			
Volume ^b	7.5 cm ³ (6.6-8.8)	8.1 cm ³ (7.2-9.2)	0.168 ^d
D98% ^b	19.1 Gy (3.1-26.0)	10.0 Gy (4.0-24.4)	0.718 ^d

<i>D2%^b</i>	53.7 Gy (32.8-59.1)	55.8 Gy (28.3-58.1)	0.622 ^d
<i>D50%^b</i>	25.9 Gy (11.2-40.1)	26.7 Gy (15.3-41.8)	0.882 ^d
<i>Dmin^b</i>	17.0 Gy (2.8-24.6)	8.6 Gy (3.2-21.9)	0.522 ^d
<i>Dmax^b</i>	57.4 Gy (42.7-59.7)	58.3 Gy (33.6-59.4)	0.718 ^d
<i>Dmean^b</i>	26.6 Gy (17.9-42.1)	29.6 Gy (17.4-41.7)	0.908 ^d

Online Resource 2 Clinical, biological and dosimetric factors associated with the development of AAL at nadir.

Abbreviations: AAL, acute absolute lymphopenia (< 1000 cells/mm³); CI, confidence interval, MGMT, O6-methylguanine-DNA-methyltransferase; RT, radiotherapy; CT, chemotherapy; FUP, follow-up; GTV, gross tumor volume; CTV, clinical target volume; PTV, planning target volume; VMAT, volumetric modulated arc therapy; Dmax, maximal dose; Dmean, mean dose; Dmin, minimal dose; D98%, dose administered to 98% of volume; D95%, dose administered to 95% of volume; D50%, dose administered to 50% of volume; D2%, dose administered to 2% of volume; V50, volume that received 50Gy; cm³, cubic centimeter; Gy, gray; b/w, between

^a Median value (95% interval of confidence)

^b Median value (I – III quartile)

^c Fisher's exact test

^d Wilcoxon sum rank test

* Variables statistically significant (p value < 0.05)